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DEPARTMENT OF THE ARMY
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On the nature of the small splenic vessels.

by G. Herzheimer.

Berliner Klinische Wochenschrift, 4: 82-84 (1917).

In addition to the usual senile atherosclerosis, the degenerative-sclerotic processes of the small and smallest vessels deserve attention due to the alteration of essential organs dependent upon them, and their significance for the general conditions of circulation. As is well known, the most important changes are those of the small renal vessels; they have a special relation to hypertonia -- in which connection the question as to cause and effect shall be ignored —; they cause, on the other hand, particularly severe degenerative renal changes leading to nephrosclerosis, i.e. customarily known as the genuine form, now called genuine angiosclerotic nephrosclerosis or nephrocirrhosis arteriolosclerotica (in contrast to arteriosclerotica," which is based on the usual senile atherosclerosis), in order to stress the importance of the small vessels in this renal affection. Concerning this renal affliction, which is accompanied by severe hypertonia, I and other authors --- Jores, Fahr, Gaskell, etc.--- have reported that the change in the small vessels in these cases may simultaneously be duplicated in other organs --- though to a lesser degree. The cerebral hemorrhages which so often represent the cause of death in such cases, are thus explained, although it is precisely in the small vessels of the brain that I failed to find alterations, which leads me to assume that even in minimally changed vessels the very high blood pressure causes hemorrhages. I have stressed the pancreas as an organ in which arteriolar changes coexist with relative frequency, in agreement with Fahr. I have seen the same in the liver. Frequently the spleen is involved, and the changes of its small vessels are similarly explained in cases of hypertonia. No doubt this also happens in the spleen. But far more frequently a slightly different hyaline thickening of the small vessels is found, and this quite often not only in cases of hypertonia. I therefore used particular caution in the inclusion of vascular changes of these splenic cases, and I find a similar differentiation and reserved evaluation in the case of Fahr, as I noted later. However, since ordinarily these vascular changes of the spleen, belonging to another category, apparently are often equated with those of other organs in the cases mentioned above, and are admitted to consideration, it seemed important to me to investigate this change of the small splenic vessels in a large amount of material, in order to clarify the incidence and nature of these changes. I therefore caused sections from a large number of spleens to be collected for several years, stained according to van Gieson for fibers, for fat and, in part, according to Bielschowsky. I then investigated the small vessels. The following is a brief report on the statistically tabulated material.

I compared a total of 1,140 spleens from persons of all possible ages and diseases. Among these, 600 = 53% show changes in their small vessels. The small arteries in the trabeculae after their "brush-like" partition are particularly involved here, as are the smallest pre-capillary arteries. The change which I found here with great frequency consists in the strong thickening and bulging of the vascular wall on the inside, presenting a regular hyaline character. With van Gieson's stain, these masses at times show an orange hue in their early stages, the pronounced lesion reveals an intensely yellow coloration; nuclei are not observed. In the case of high-grade alterations, especially, the masses either surround the lumen uniformly on all sides, whether the lumen is affected longitudinally or across, or (as is also found frequently) it is more unilaterally located in a smaller or larger area of the periphery of such a bulging hyaline part. The endothelium is situated toward the interior, often collapsed, since the lumen usually is very narrow, frequently closed entirely. In the case of very small vessels, these hyaline masses are bordered on the outside by slightly red (van Gieson) connective tissue; in slightly larger arteries equipped with a thin muscular layer this at times occurs outside of the hyaline mass, even if compressed; in such cases the hyaline may have originated with the connective tissue. It becomes apparent most of all by means of these small arteries, which carry a thin muscular layer, that the latter turns into the hyaline mass, accompanied by the loss of its nuclei and enlargement. Only the endothelium is then found on the inside, the exterior consists at most of thin adventitial connective tissue. The whole process evidently has a degenerative character. In the case of advanced lesions particularly, those of the splenic vessels resemble those of the renal arterioles in hyper-tonia, which I used as point of departure. In the spleen, however, the slightly larger vessels are predominantly involved, and accordingly the muscularis contributes the greatest share to the hyaline mass. This may explain the circumstance that, while van Gieson's stain produces the same picture of hyaline yellow masses, the latter show a divergent reaction with fatty stains (scarlet R). Intense, almost diffuse red coloration in the smallest renal vessels; here in the spleen the same is at times seen, but only very fine fatty granules, sometimes missing altogether. Incidentally, Poscharisky (Ziegler's Beitr., 1912, Vol. 54) has already described the fat content of the hyaline-degenerated small splenic vessels.

No special results were obtained by staining for elastic fibers. The smaller arteries have none and those of the larger ones as well as the elastic fiber network surrounding the small splenic vessels were mainly unchanged. Still, the elastic fibers in the region of the hyaline vessels seemed decidedly separated and decreased,

The described hyaline degeneration of the small vessels was found not only in individual vessels --- had I counted these cases, the number of those with vascular lesions would have been greater --- but always in a large number of affected vessels, even though variable in extent. In the vast majority of cases that showed changes to a higher degree, hardly any small vessels were spared. Usually the process is

widely distributed, although subject to individual variations. The same is true for the degree of change. I have attempted a classification in cases with minimal hyaline vessels --- in which the thickening and the hyaline nature are distinct but scant, and frequently not widely distributed --- into average cases and those with severe changes, where nearly all small arteries present lesions in a manner immediately noticeable.

Upon statistical tabulation of 640 spleens of the appropriate description, I have found 205 cases = 34% with sparse occurrence, 184 cases = 31% with average and 211 cases = 35% with strong or very strong representation. The distribution is rather even.

It was desirable, first of all, to distribute the result on various age brackets. I enclose a tabulation calculated in percent.

Age	No vascular changes	Vascular changes	Minimal lesions	Average lesions	Severe lesions
1-10	85	15	10	3	2
10-20	58	42	28	9	5
20-30	57	43	20	13	10
30-40	48	52	20	20	12
40-50	34	66	23	25	18
60-70	25	75	14	17	44
70-80	12	88	20	31	37
over 80	8	92	20	36	36

In scanning the table, we note that the number of positive cases, i.e. those showing vascular changes, increases in almost a direct line with advancing age (the one small reversal in the seventh decade is surely accidental). Concerning the intensity, we find that the average and severe changes also increase in number almost in direct linear proportion, even though the distribution in the last decades remains more uniform.

Expressed in words, one might say: The small arteries of the spleen in children under 10 are generally unchanged, a minimal hyaline character is a rare exception. But already at over 10 until 40 years of age, the vascular alteration is present in about one-half of all individuals, often to a high degree. From 40-70 years, it is found in 2/3 to 3/4 of all persons, in about one-half to a higher degree, and is almost invariably present in more advanced age, predominantly in a high degree of intensity.

It now appeared of further interest to consider statistically the diseases which had afflicted the individuals or had been their cause of death. Since this failed to reveal any kind of system or law, I shall not reproduce the tables here and only sum up briefly. Among the chronic diseases, I first considered tuberculosis or pulmonary TB. The percentages of negative and positive cases corresponded closely to the general tabulation. In any case, the average number of those with

altered vessels was not greater among tuberculous persons than in general, not even in the younger age group. The same is true, assuming that the small number of my cases permits an evaluation, of syphilitic persons; the vessels were intact almost without exception, especially in the case of congenital syphilis of small children. Of the acute infectious diseases, pneumonia, typhus and diphtheria were considered. Here, too, the proportion of vascular affections in the individual age groups failed to deviate essentially from average values. The same conditions were tabulated for malignant tumors as well as cases of diabetes, without gaining a clue to the influence of these diseases. Even in 29 persons of diverse ages who died suddenly in accidents, the vessels were altered in the same manner as in persons who succumbed to various diseases.

Finally, it seemed important to compare individuals who, during autopsy, revealed a particularly high grade of atherosclerosis. I had sufficient material for comparison only from age 50 on. It was shown that here the changes of the small or smallest vessels indeed occurred more frequently and were of a higher degree in comparison to the average, but the deviation was not very pronounced. In the vast majority of cases with lesions of the small splenic vessels —— this is apparent from their number and from the youthful age groups —— a stronger, general atherosclerotic change of the larger vessels is not present at the same time, nor do the larger splenic vessels show an atherosclerotic picture. This may, of course, be the case especially in the higher age groups, but it does not occur as a rule; at any rate, no parallel can be established between atherosclerotic alterations of the larger splenic vessels and the affection of the small ones being discussed here. This agrees with the opinion of Aschoff et al. about the behavior of the large vessels in cases of hypertonia with changes of the smallest renal vessels, as also confirmed by me some time ago.

Naturally, the hyaline changes of the small splenic vessels do not belong in the category of ordinary atherosclerosis. Nor can we speak of a "pre-senile" type, since they are already present in nearly every second person beginning with the second decade. As stressed especially by Aschoff, other organs reveal a more isolated, earlier occurring vascular alteration which may be attributed to functional performance. In particular, he mentions the uterus and the ovaries. But here the arteries are larger than those under consideration in the spleen, and the change is histologically quite different. In addition, the vascular changes associated with menstruation and pregnancy, although occurring relatively early, arise far later than in the spleen. And yet I believe that, in so far as a tertium comparationis exists with the changes of the small splenic vessels statistically investigated by me, these too must be explained as a sign of functional attrition or adaptation. Despite their frequency we cannot consider them to be physiological, they do not accompany certain diseases, their only connection with age is an increase in frequency. Thus only a local functional correlation remains. And here the frequency and the youthful occurrence of the vascular affection may

give us an indication to consider the locale, i.e. the peculiar vascular and capillary conditions of the spleen and possibly even the function of the spleen, which has such a close relationship with the vascular system and the blood. If we consider the highly similar changes of the small and smallest vessels of the kidney (and other organs) in the case of hypertonia not as the cause but the effect of high blood pressure --- although subsequently elevating it --- one could think of the elevated splenic blood pressure as sufficient cause for the alteration of the small vessels. In that case this increased blood pressure would not represent general hypertonia, but local hypertonia of the spleen, related to its special circulatory conditions. This or a similar explanation which involves physiological conditions would clarify the frequency and early occurrence of the conspicuous behavior of the small splenic vessels, as has been presented above in more detail. Apparently these vascular conditions have no disadvantageous effects on the spleen or the total organism.

To return to the starting point of my investigations, it follows from my presentations that we may consider the described hyaline degeneration of the small splenic arteries as a special condition, and may not include it in the evaluation of vascular changes found in cases of general hypertonia in the kidney and other organs. They are present far too generally in cases without hypertonia. I have found the corresponding change in the small splenic vessels in the spleen of 10 cases of hypertonia with genuine angiosclerotic nephrosclerosis, available to me here, and in 9 out of 10 cases the condition was high grade. It is quite possible that, if the circulatory conditions in the spleen are physiologically favorable to vascular change, as discussed above, this occurs the more so if general hypertonia is present as an additional factor, and that possibly vascular alterations are found more generally in connection with hypertonia, especially in the spleen. Considering the frequency of an identical state of the splenic vessels in other cases, no diagnostic or similar significance may be ascribed to these changes, at least those relating to the hyaline degeneration of the larger splenic arteries, and under no circumstances when hypertonia is involved.

I have not touched on the literature concerning the problem at hand. At this time I am unable to do so. The literature contains many a report on the action of the splenic vessels and hyaline arteria changes have often been noted by numerous investigators. In 1912 Tsunoda read a paper about them before the Japanese Pathological Society. However, the report is very short and not clear. Tsunoda compared amyloid and hyaline degeneration of the splenic vessels and follicles in 380 spleens and considers them to be a sequel of marantic diseases, especially carcinoma, tuberculosis, lues. Fahr, in his studies of nephrosclerosis and arteriosclerosis of the small organ arteries (1), departing from the same point as I, as discussed in the introduction, pointed to the frequency of a hyaline degeneration of the "vascular wall of the small arteries of the splenic penicillus, in which an origin in the hyperplastic intimal thickening is not clearly indicated." He also segregates, and rightly so, hyperplastic thickening of the intima

from hyaline degeneration of the splenic penicillus arteries. I am not acquainted with a more precise, statistical representation of hyaline degeneration of the small splenic arteries. Such a tabulation seemed indicated to me, especially in view of the problem of hypertonia, as already stated.

Finally it should be mentioned briefly that often the fine capillaries of the splenic follicles also are involved in thickening of the walls of hyaline appearance. They stain red with van Gieson and usually are accompanied by hyaline thickening of the reticular "gitter fibers" of the follicles. A thin exudate also points to the changes in these capillaries. At the same time, reticular cells have often proliferated in the form of socalled vesicular cells of the follicles. These alterations of the capillaries shall only be touched on here --- they have no bearing on the question discussed above ---; perhaps I shall return to them elsewhere.

NOTE.

(1) Frankf. Zschr. f. Path., Vol. 9, 1911.